bacteriocidal/permeability increasing protein (BPI) or a hybrid of LBP [with the LPS] and a lipopolysaccharide binding site of [the] limulus anti-[LPS] lipopolysaccharide factor (LALF).

33. (Amended) The process of claim 28, wherein said [vatiants and/or mutants of] LBP [are point-mutated variants the functions of which are improved at the LPS binding site (amino acids 91-101) by individual exchanges of amino acids] comprises one or more point mutations which increases the binding affinity of LBP for lipopolysaccharide.

REMARKS

Claims 28-33 are pending in the application. Applicants thank the Examiner for examining claims 28-33.

In order to obviate the Examiner's objections, Applicants have amended claims 28, 31 and 32 as suggested by the Examiner.

In response to the rejections under 35 U.S.C. § 112, second paragraph, Applicants have amended claims 28, 32 and 33 to more particularly point out and distinctly claim the subject matter which Applicants regard as their invention. In particular, Applicants have amended claim 28 to more particularly point out that the process of the invention includes administering an effective amount of LBP to a patient in need therefor. In addition, Applicants have amended claims 32 and 33 to more particularly point out that "LPS" refers to "lipopolysaccharide" and to correct errors in antecedent bases resulting from the amendments to claim 28. Support for all amendments can be found in the specification and claims as originally filed.

The Applicants respectfully traverse the Examiner's rejections of claims 28, 32 and 33 and of claims 29-31 under 35 U.S.C. § 102(b) as anticipated by WO 94/25476 ("Scott"), as well as the Examiner's rejection of claims 29-31 under 35 U.S.C. § 103(a) as obvious over Scott. Scott describes the influence of bacteriocidal permeability increasing protein (BPI) variants, lipopolysaccharide binding protein (LBP) variants, and BPI-LBP chimeras, on LPS-mediated activity. Table 1 on page 9 of Scott indicates that BPI inhibits LPS-mediated activity, whereas LBP stimulates LPS-mediated activity. Scott discloses that LBP binds to LPS and stimulates monocyte activation, which in turn causes the release of deleterious quantities of cytokines (page 8, lines 15-17). Thus, Scott proposes the development of LBP variants and LBP-BPI chimeras that possess an LPS binding activity and a longer half-life than native LBP in order to inhibit LPS-mediated activity.

In contrast, the present invention surprisingly shows the result that LBP inhibits LPS-mediated activity *in vitro* and *in vivo* and can be used as a therapy for LPS-mediated ailments. Scott neither teaches nor suggests the inhibitory activity of LBP on LPS-mediated activity, nor does it render obvious that teaching. In fact, Scott teaches away from the present invention by demonstrating the stimulatory activity of LBP on LPS-mediated activity.

The Applicants also respectfully traverse the Examiner's rejection of claims 28 and 33 under 35 U.S.C. § 102(b) as anticipated by WO 95/08560 ("Heavner"). Heavner describes the use of LBP-derived peptides for treating sepsis by inhibiting the LBP-LPS interaction (see page 5, line 7 and Figure 3). However, Heavner only describes the use of

peptides derived from LBP, and not of the entire protein. Therefore, Heavner does not anticipate the use of the entire LBP molecule to treat sepsis or any other LPS-mediated ailment.

In view of the foregoing, reconsideration of the outstanding rejections, and the allowance of claims 28-33 are respectfully urged.

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Respectfully submitted,

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It is hereby certified that this is bening mailed on January 17, 2003

Francene Sawyer